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Criteria for Shortage Probability:

Vaccines are assumed to 4 categories or scenarios based for shortages based on the number of manufacturers for a particular vaccine type, the stability of the market for that vaccine type, history of problems with manufacturing, projects changes in the market or vaccine type in the near future and complexity in production.

The scenarios are described as follows:

Scenario 1: Two manufacturers, a relatively stable market, no recent history of production problems, and no projected changes vaccine type or recommendations in the near future.
Scenario 2: Two manufacturers, but a slightly higher potential of production problems due to either new or changing market, recent history of manufacturing problems, projected changes in the vaccine type in the near future, or relative complexity of production process.
Scenario 3: One manufacturer, a relatively stable market, no recent history of production problems, and no projected changes vaccine type or recommendations in the near future.
Scenario 4: One manufacturer, but a slightly higher potential of production problems due to either new or changing market, recent history of manufacturing problems, projected changes in the vaccine type in the near future, or relative complexity of production process.

Based on those scenarios, the following criteria were used to determine assumptions for probabilities of different degrees of shortages:

0% Shortage Probability: Vaccine types with a relatively stable market and production are given a probability of 0.3 while those vaccine types with a slightly higher potential of production problems have a lower probability of a 0% shortage of 0.2.
25% and 50% Shortage Probability: Vaccine types with two manufacturers are given a probability of 0.2 while those vaccine types with one manufacturer have a slightly lower probability of 0.15.
75% Shortage Probability: Vaccine types with a relatively stable market and production are given a probability of 0.2 while those vaccine types with a slightly higher potential of production problems have a higher probability of a 0% shortage of 0.3.
100 % Shortage Probability: Vaccine types with two manufacturers are given a probability of 0.1 while those vaccine types with one manufacturer have a slightly higher probability of 0.2.

Below is a summary of the scenarios and shortage probabilities.

Scenario Table

	0% Shortage Probability	25% Shortage Probability	50% Shortage Probability	75% Shortage Probability	100% Shortage Probability	SUM of Probabilities
Scenario 1	0.30	0.20	0.20	0.20	0.10	1.00
Scenario 2	0.20	0.20	0.20	0.30	0.10	1.00
Scenario 3	0.30	0.15	0.15	0.20	0.20	1.00
Scenario 4	0.20	0.15	0.15	0.30	0.20	1.00

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Hepatitis B Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: HepB vaccine is a 3-dose schedule recommended starting at birth.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. Since the stockpile currently has a 2 million dose target for the combination vaccine DTaP-HepB-IPV, the 'High' HepB target is 6 million doses (from the cohort calculation) minus 2 million doses = 4 million doses and since there are 4 million doses of the HepB vaccine delivered to the stockpile, the 'Low' target is 2 million doses (50% of the 'High' target). Note that there is also a 1 million dose target for the combination vaccine HepB-Hib; however this target dose quantity was not subtracted from the cohort calculation for the HepB target.
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there are 2 manufacturers (lower risk of 100% shortage) and a relatively stable market without recent supply problems or projected market changes. See Scenario 1 in Criteria for Shortage Probability addendum.
Step 8: The estimates are based on the most likely estimate of the number of children born to HBsAg positive women of 23,919 with a low estimate of 16,187 (2004 CDC unpublished data). The estimated average rate of hepatitis B virus infection in an infant born to a HBsAg positive mother in the absence of vaccine = 42% (Armstrong GL et al. Childhood hepatitis B virus infection in the United States before hepatitis immunization. Pediatrics 2001;108:1123-1128). The most likely and low rates are calculated from the estimated birth cohort of 4.2 million.
Step 9: The estimates are based on the estimate that 90% of children infected at birth will develop chronic HBV infection (Armstrong GL et al. Childhood hepatitis B virus infection in the United States before hepatitis immunization. Pediatrics 2001;108:1123-1128).
Step 10: The estimates are based on the estimate that 25% of those with chronic HBV will result in death from chronic liver disease (cirrhosis or hepatocellular carcinoma) (Armstrong GL et al. Childhood hepatitis B virus infection in the United States before hepatitis immunization. Pediatrics 2001;108:1123-1128).
Step 11: Vaccine efficacy is based on a protective hepatitis B surface antibody (anti-HBs) level in vaccinated infants and that now cases of clinincal hepatitis B have been observed in 10-22 year follow-up studies among immunocompetent vaccinated populations (Shepard CW et al. Hepatitis B inflection: Epidemiology and Vaccination. Epidemiologic Reviews 2006;28:112:125).
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the average of ENGERIX® (GSK) and RECOMBIVVAX® (Merck) of $9.63 per dose. It does not consider the price at the time of vaccines already delivered to the stockpile.

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Rotavirus Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.

Step 2: Rotateq® (Merck) is a 3-dose schedule and Rotarix® (GSK) is a 2-dose schedule. The model uses the 3-dose schedule and the 3-dose vaccine price. The price per vaccine series is roughly equivalent for either vaccine ($171.60 for the 3-dose vaccine and $164.56 for the 2-dose vaccine based on the CDC contract price on August 1, 2008), so the assumption will not affect the overall vaccine costs regardless of which vaccine is stockpiled.

Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. A 6 million dose High Target is used for Rotavirus vaccine (based on a 3 dose schedule) and currently there are 2.5 million doses of the 3-dose Rotavirus vaccine delivered to the stockpile.

Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007. All the doses distributed in 2007 are the 3-dose vaccine from Merck as GSK's vaccine was licensed in 2008.

Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).

Step 6: Probability degrees of shortages in Step 5 based on the fact that there are 2 manufacturers (lower risk of 100% shortage), but some increased risk of supply disruptions due to the recent introduction of the vaccine(s), competition with unknown steady state market share, and relative complexity of manufacturing a live virus vaccine. See Scenario 2 in Criteria for Shortage Probability addendum.

Steps 8 - 10: These are estimates of risk of outcome by age 59 months if unvaccinated, and are based on estimates from pre-vaccine era (2004). The assumption is that at this time there is no herd immunity from vaccinated population. The estimate for the most likely rates is the median estimate with the low estimate being the 5th percentile estimate and the high estimate being the 95th percentile estimate (Widdowson M-A, Meltzer MI, Zhang X, Bresee JS, Parashar UD, Glass RI. Cost-effectiveness and potential impact of rotavirus vaccination in the United States. *Pediatrics.* 2007;119(4):684-697).

Step 11: Vaccine efficacy is based results form clinical trials and results in the U.S. over approximately 2 seasons (Widdowson M-A, Meltzer MI, Zhang X, Bresee JS, Parashar UD, Glass RI. Cost-effectiveness and potential impact of rotavirus vaccination in the United States. *Pediatrics.* 2007;119(4):684-697) (Vesikari T, Matson DO, Dennehy P, et al. Safety and efficacy of a pentavalent human-bovine (WC3) reassortant rotavirus vaccine. *N Engl J Med.* Jan 5 2006;354(1):23-33) (Vesikari T, Karvonen A, Prymula R, et al. Efficacy of human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in European infants: randomised, double-blind controlled study. *Lancet.* Nov 24 2007;370(9601):1757-1763). Data on efficacy against mortality is not available; efficacy was assumed to be equal to efficacy againt hospitalization.

Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the 3-dose vaccine of $57.20 per dose. It does not consider the price at the time of vaccines already delivered to the stockpile.

Diphtheria and Tetanus (pediatric) Inputs:

The assumption was made to model for DTaP/Tdap utilizing pertussis inputs because pertussis has a significantly higher disease burden than diphtheria and tetanus is non-communicable. The impact from diphtheria would be difficult to quantify because of the rarity of endemic disease; no reported cases of indigenous diphtheria in the U.S. since 2000 or imported cases since 2003. Therefore, the results from a shortage of DTaP/Tdap vaccine would be detected far earlier for pertussis than diphtheria.

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Pertussis (pediatric) Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: DTaP is a 5-dose schedule recommended at age 2, 4, 6, and 15-18 months plus a preschool dose at age 4-6 years.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. Since the stockpile currently has a 2 million dose target for the combination vaccine DTaP-HepB-IPV, the 'High' DTaP target is 10 million doses (from the cohort calculation) minus 2 million doses = 8 million doses. Currently there are 1.5 million doses of the DTaP vaccine delivered to the stockpile.
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there are 2 manufacturers (lower risk of 100% shortage), but some increased risk of supply disruptions due to the recent introduction of the combination vaccine(s) and competition with unknown steady state market share. See Scenario 2 in Criteria for Shortage Probability addendum.
Step 8: The low incidence is based on the current average incidence from U.S. surveillance data among children <5 years of age (CDC unpublished data). The most likely estimate is based on the reported rate for infant's ≤2 months of age (M. Tanaka; C. Vitek; F. Pascual; et al. Trends in Pertussis Among Infants in the United States, 1980-1999. JAMA. 2003;290(22):2968-2975). The high rate is based on available pre-vaccination era data (Cherry, J. Pertussis in the Preantibiotic and Prevaccine Era, with Emphasis on Adult Pertussis. CID 1999;28 (Suppl 2): S107–1.
Step 9: The low estimate is based on reported data for infants age 7-11 months of age and the high estimate is based on reported data for infants in the first month of life (M Cortese, A. Baughman, et. al. Pertussis hospitalizations among infants in the United States, 1993 to 2004. Pediatrics. 2008 Mar;121(3):484-92). The most likely rate is based on U.S. surveillance data (CDC. Pertussis --- United States, 2001—2003. MMWR 54(50);1283-1286).
Step 10: The low estimate is based on the average of the case fatality rate for infants age 6-11 months of age reported in 2006 and 2007 and the mostly likely estimate is based of the reported rates for ages <1 year of age for the same period (CDC unpublished data). The high estimate is based on the reported rate for infants <2 months of age (CDC. Preventing tetanus, diphtheria, and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine: Recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. MMWR 2006;55(No. RR-17)).
Step 11: The low and most likely estimate for vaccine effectiveness against disease is based on the reported effectiveness of 1-2 doses of DTaP among children 6-59 months of age in the U.S. and the high estimate is based on the reported effectiveness of ≥4 doses in the same group (K. Bisgard, P. Rhodes, B. Connelly, et. al. Pertussis Vaccine Effectiveness Among Children 6 to 59 Months of Age in the United States, 1998–2001. Pediatrics 2005;116;e285-e294). The estimate of vaccine effectiveness against hospitalization is based on the marked decrease in hospitalization rate from age 1 month to age 3 month suggesting protection with even 1 dose of DTaP (M Cortese, A. Baughman, et. al. Pertussis hospitalizations among infants in the United States, 1993 to 2004. Pediatrics. 2008 Mar;121(3):484-92). The most likely rate is based on U.S. surveillance data (CDC. Pertussis --- United States, 2001—2003. MMWR 54(50);1283-1286). The effectiveness against death is an approximation based on surveillance data suggesting the majority of deaths occur in infants who have not received any doses of DTaP (CDC unpublished data).
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the average of Infanrix® (GSK) and Daptacel® (Sanofi) of $13.50 per dose. It is assumed that Tripedia® (Sanofi) would not be placed in the stockpile. It does not consider the price at the time of vaccines already delivered to the stockpile.

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DTaP-HepB-Hib Inputs:

Step 1: The 'High' target is based on the current target for this combination vaccine that contributes to the total target for DTaP, HepB, and Hib based on the cohort method. Note that since there are currently two combination vaccines in the stockpile the contain HepB, the total HepB target is higher than the cohort method would calculate. 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. Currently there are 500,000 doses of the DTaP-HepB-IPV vaccine delivered to the stockpile.
Step 2: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 3: Price based on the 2008 CDC contract as of August 1, 2008.

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Hib Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.

Step 2: ActHIB® (sanofi) is a 4-doses schedule and PedvaxHIB® (Merck) is a 3-dose schedule. The model uses the 4-dose schedule and the 4-dose vaccine price. The price per vaccine series is roughly equivalent for either vaccine ($34.56 for the 4-dose vaccine and $33.78 for the 2-dose vaccine based on the CDC contract price on August 1, 2008), so the assumption will not affect the overall vaccine costs regardless of which vaccine is stockpiled.

Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. Since the stockpile currently has a 1 million dose target for the combination vaccine Hib-HepB, the 'High' Hib target is 8 million doses (from the cohort calculation) minus 1 million doses = 7 million doses. Currently there are 380,000 doses of the 3-dose Hib vaccine delivered to the stockpile (this does not include vaccine that was recalled that will need to be replaced when available).

Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007. All the doses distributed in 2007 which includes both 4-dose and 3-dose series vaccine.

Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).

Step 6: Probability degrees of shortages in Step 5 based on the fact that there are 2 manufacturers (lower risk of 100% shortage), but some increased risk of supply disruptions due to the recent recall of vaccine from one of the manufacturers and the recent introduction of a combination vaccine containing Hib providing competition with unknown steady state market share. See Scenario 2 in Criteria for Shortage Probability addendum.

Step 8: The low estimate is based on the rate of *Haemophilus influenzae* type b disease among children <5 years of age in the U.S. in 1987 prior to the implementation of Hib conjugate vaccine (Progress Toward Eliminating Haemophilus influenzae Type b Disease Among Infants and Children -- United States, 1987-1997. MMWR. 1998 / 47(46);993-8). The most likely estimate is based on the average of the rate of 60-100 cased per 100,000 among children <5 years of age in the U.S. in the pre-vaccine era (Broom CV. Epidemiology of *Haemophilus influenzae type* b infections in the United States. Pediatr Infect Dis J 1987;6:779-82); (Ward J. Leiberman JM, Cochi SL. Haemophilus influenzae vaccines. In Plotkin SA, Mortimer EA, editors. Vaccines. 2nd ed. Philadelphia: WB Saunders Co; 1994. p 337-86). The high estimate is base on rates among unvaccinated Native Americans <5 years of age (Singleton R., Bulkow L., Levine O., et al. Experience with the prevention of invasive Haemophilus influenzae type b disease by vaccination in Alaska: The impact of persistent orpharyngeal carriage. Pediatrics 137:3: 313-20).

Step 9: The range of rates is based on the range reported in the U.S. from 1980-1991 (Kenneth C. Schoendorf, John L. Kiely, William G. Adams, and Jay D. Wenger. National Trends in *Haemophilus influenzae* Meningitis Mortality and Hospitalization among children, 1980 through 1991. Pediatrics 93:4:663-68).

Step 10: The range of rates is based on the range reported in the U.S. in the pre-vaccine era (CDC. Epidemiology and Prevention of Vaccine Preventable Diseases, *Haemophilus influenzae*. 8ed. 2004; Recommendation of the Immunization Practices Advisory Committee (ACIP) Polysaccharide Vaccine for Prevention of Haemophilus influenzae Type b Disease. MMWR. 1985 / 34(15);201-5); Current Trends Prevention of Secondary Cases of Haemophilus influenzae Type b Disease. MMWR 1982 / 31(50);672-674,679-680).

Step 11: The most likely and high estimates are based on the range of development of protective antibody levels after a primary series of 2-3 doses. The low estimate is an approximation of vaccine effectiveness under less than ideal conditions.

Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the 4-dose vaccine of $8.64 per dose. It does not consider the price at the time of vaccines already delivered to the stockpile.

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Hib*HepB Inputs:

Step 1: The 'High' target is based on the current target for this combination vaccine that contributes to the total target for HepB and Hib based on the cohort method. Note that since there are currently two combination vaccines in the stockpile the contain HepB, the total HepB target is higher than the cohort method would calculate. 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. Currently there are 200,000 doses of the HepB-Hib vaccine delivered to the stockpile (this does not include vaccine that was recalled that will need to be replaced when available).
Step 2: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 3: Price based on the 2008 CDC contract as of August 1, 2008.

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Pneumococcal Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: PCV is a 4-dose schedule recommended at age 2, 4, 6, and 12-15 months.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. A 8 million dose High Target is used for PCV7 vaccine (based on a 4 dose schedule) and currently there are 1.75 million doses delivered to the stockpile.
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there is 1 manufacturer (higher risk of 100% shortage) with some increased risk of supply disruptions given the expectation of one or more next generation pneumococcal vaccines in the near future and the complexity of manufacturing multiple antigen conjugate vaccines. The production issues in the recent past were not taken into consideration because the source of those issues have been addressed. See Scenario 4 in Criteria for Shortage Probability addendum.
Step 8 – 10: The low estimates are based on vaccine-type pneumococcal disease currently for children less that 5 years of age. The most likely estimates are based on the rate in 2002 (early in the introduction of vaccine and during supply interuptions), and the high estimates are based on the pre-vaccine era rate (CDC. Invasive pneumococcal disease in children 5 years after conjugate vaccine intorduction – eight states, 1998-2005. MMWR 2008; 57:144-8) (ABC Surveillance Reports 1998-2007 – http://www.cdc.gov/ncidod/dbmd/abcs/survreports.htm).
Step 11: Efficacy against vaccine type invasive disease estimates and 95% confidence intervals are based on clinical trial data (Black S, Shinefield H, Fireman B, Lewis E, Ray P, Hansen JR. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. *Pediatr Infect Dis J.* 2000;19:187-195) (Whitney CG, Pilishvili T, Farley MM, Schaffner W, Craig AS, Lynfield R, et al. Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: a matched case-control study. Lancet 2006;368(9546):1495-502). Efficacy against hospitalization and mortality is based on the assumption that vaccine prevents disease entirely (rather than modify disease).
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the PCV7. It does not consider the price at the time of vaccines already delivered to the stockpile.

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Polio Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: IPV is a 4-dose schedule recommended at age 2, 4, 6-18 months, and 4-6 years.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. Since the stockpile currently has a 2 million dose target for the combination vaccine DTaP-HepB-IPV, the 'High' IPV target is 8 million doses (from the cohort calculation) minus 2 million doses = 6 million doses. Since there are 3.655 million doses of the MMR vaccine delivered to the stockpile, the 'Low' target is 3 million doses (50% of the 'High' target).
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there is 1 manufacturer (higher risk of 100% shortage) with some increased risk of supply disruptions given the increase in the number of combination vaccines with IPV in the formulation and a market that is not at steady state. See Scenario 4 in Criteria for Shortage Probability addendum.
Step 8: The low estimate is based on a scenario where there was no introduction of wild-type polio virus into the U.S. The most likely rate is based on the case rate for polio in 1981. The high estimate is based on the current rate in Nigeria.
Step 9: The hospitalization rates are based the assumption that in the current era, most, if not all polio cases would be hospitalized for some period of time in the U.S.
Step 10: The low estimate for case fatality rate is based on rates in developing countries (Wyatt HV "Differential Diagnosis of acute flaccid paralysis: poliomyelitis in developing countries (http"///www.ias.ac.in/no 10/articles21.htm accessed on August 22, 2008). The most likely rate is based on case reports between 1969 and 1981 in the U.S (1980-1981 CDC Poliomyelitis Surveillance Report). The high rate is based on data from an outbreak in Cape Verde in September 2002.
Step 11: Efficacy estimates are based on low, average, and high antibody responses to any of the three poliovirus types (Vaccines, 5th ed. Table 25-4, p 610).
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the IPV. It does not consider the price at the time of vaccines already delivered to the stockpile.

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Measles Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: MMR is a 2-dose schedule recommended at age 12-15 months and 4-6 years.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. The 'High' target is 4 million doses (from the cohort calculation) and since there are 4 million doses of the MMR vaccine delivered to the stockpile, the 'Low' target is 2 million doses (50% of the 'High' target).
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there is 1 manufacturer (higher risk of 100% shortage) with some increased risk of supply disruptions given the supply disruptions in 2001-02, the possibility of one or more combination products containing MMR in the near future, and relative complexity of manufacturing a live virus vaccine. See Scenario 4 in Criteria for Shortage Probability addendum.
Step 8: The low estimate is based on published U.S. data of with established vaccine coverage (CDC. Measles—United States 2000. *MMWR.* 2002; 51: 120-3; also Harpaz R, Papania MJ, Fujii KE, et al. Lessons learned from establishing and evaluating indicators of the quality of measles surveillance in the United States, 1996-1998, *J Inf Dis.* 2004; 189: S196). The most likely estimate is based data from the 1989-91 resurgence (*MMWR,* Current trends measles—United States, 1989 and first 20 weeks 1990). The high estimate is based on applying the resurgence rates to the entire U.S. birth cohort. Measles is the most infectious disease known and in the pre-vaccine era affected the entire birth cohort. (Harpaz R. Completeness of measles case reporting: review of estimates for the United States. *J Inf Dis. 2004;* 189: S185.)
Step 9: The low estimate is based upon percent of cases affected with severe complications, e.g., 1-6% of cases acquire pneumonia with established vaccine coverage. (Strebel PM, Papania MJ, Dayan GH, Halsey NA *Vaccines,* Measles vaccine chapter). The most likely estimate is based upon hospitalization data from the 1989-1991 measles resurgence (*MMWR,* Current trends measles—United States, 1989 and first 20 weeks 1990). The high estimate is based upon an estimated rate that doubles the rate that occurred during the 1989-91 resurgence.
Step 10: The low estimate is based on the mortality rate with established vaccine coverage (Strebel PM, Papania MJ, Dayan GH, Halsey NA *Vaccines,* Measles vaccine chapter). The most likely rate is based upon data from the 1989-1991 measles resurgence (*MMWR,* Current trends measles—United States, 1989 and first 20 weeks 1990). The high rate is based upon the case fatality rate reported during outbreaks in refugee camps (Heymann, *Control of Communicable Diseases Manual, 18th ed.*).
Step 11: The low efficacy estimates are based on an approximation of efficacy under less than ideal conditions, the most-likely is based on 1-dose efficacy, and the high is based on 2-dose efficacy. Efficacy against hospitalization and mortality is based on the assumption that vaccine prevents disease entirely (rather than modify disease).
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the MMRII® (Merck) vaccine of $18.26 per dose. It does not consider the price at the time of vaccines already delivered to the stockpile.

Mumps and Rubella Inputs:

Vaccines for the prevention of measles, mumps, and rubella are currently stockpiled as MMR vaccine. Very small amounts of monovalent measles, mumps, and rubella vaccines are produced and distributed in the United States and there is no routine ACIP recommendation for the use of monovalent vaccines to protect from these diseases. The assumption was made to model for MMR utilizing measles inputs because measles is the most infectious of the three diseases and would have the most severe immediate implications if a shortage were to occur. Modeling utilizing rubella was considered because of congenital rubella syndrome (CRS), but it was felt that measles would be the driving force behind any decisions due to its infectiousness and the severity of its complications. The impact from rubella would also be more difficult to quantify because so many implications from CRS don't appear until later in life.

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Varicella Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: Varicella vaccine is a 2-dose schedule recommended at age 12-15 months and 4-6 years.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. The 'High' target is 4 million doses (from the cohort calculation) and since there are 2 million doses of the Varicella vaccine delivered to the stockpile which is also 50% of the 'High' target, the 'Low' target is 2 million doses.
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there is 1 manufacturer (higher risk of 100% shortage) with some increased risk of supply disruptions given the supply disruptions in 2001-02 as well as recent issues with bulk production and intermittent shipping delays, the possibility of one or more combination products containing Varicella vaccine in the near future, and relative complexity of manufacturing a live virus vaccine. See Scenario 4 in Criteria for Shortage Probability addendum.
Step 8: The low estimate is based upon the assumption that a second varicella dose further reduces breakthrough varicella by 2/3 (Kuter) compared to one dose; we also know from active surveillance sites that about 60% of the current varicella cases are among vaccinees. Therefore, a second dose is likely to reduce breakthrough cases by 40%. Furthermore, catch up vaccination and vaccine coverage are expected to increase. Therefore, the resultant rate would be expected to be reduced to 0.25 per 1000 population. The most likely estimate is based upon the 2005 incidence rate of varicella in active surveillance sites ranging from 0.4-1.1 per 1000 population with vaccine coverage approaching 90%. The 2006 National vaccine coverage among children 19-35 months of age is about 90%. Taking an average of the two rates, we expect the national rate to be 0.75/1000 population. The high estimate is based upon the pre-varicella vaccine incidence rate in the US of 16/1000 population.
Step 9: The low estimate is based data that Vaccinated children were less likely to be hospitalized (1.8 versus 6.8 per 1000 cases) when compared to unvaccinated cases. The most likely and high estimates are based upon the range of hospitalization among varicella cases in the pre-vaccine era.
Step 10: The low estimate is based upon the continued increase in varicella vaccination coverage and the current recommendations for 2-doses in addition to catch up vaccination that would be expected to result in further decline in varicella cases and mortality. Therefore, we would assume that by 2009, varicella case fatality may be further reduced by an additional 10% resulting to reach 0.30 per 100,000 cases. The most likely rate is based upon evidence that varicella mortality rates declined 87% in 2003-2005 compared to 1990-1994. If we assume a similar decline in fatality rate, then the case fatality rate would be 0.34 per 100,000 cases. The high estimate is based upon the varicella case fatality rate of 2.6 in 1990-1994.
Step 11: Efficacy estimates were based on 1-dose efficacy against any disease, 2-dose efficacy against any disease, and 1-doses efficacy against severe disease.
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the Varivax® (Merck) vaccine of $61.50 per dose. It does not consider the price at the time of vaccines already delivered to the stockpile.

APPENDIX
VacStockpile Addendum – Input Assumptions

Hepatitis A Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: HepA vaccine is a 2-dose schedule recommended starting at age 12 months.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. The 'High' target is 4 million doses (from the cohort calculation) and since there are 2.5 million doses of the HepA vaccine delivered to the stockpile, the 'Low' target is 2 million doses (50% of the 'High' target).
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there are 2 manufacturers (lower risk of 100% shortage), but some increased risk of supply disruptions due to the recent supply problems with one of the manufacturers of HepA vaccine even though the alternative manufacturer is currently able to meet the national demand for the vaccine. See Scenario 2 in Criteria for Shortage Probability addendum.
Step 8: The most likely estimate is based upon data that an estimated 51% of hepatitis A cases among children (2-18 years) are prevented by immunization, includes the effect of direct and indirect (herd) immunity (Samandari et al. Quantifying the impact of hepatitis A immunization in the United States, 1995-2001. Vaccine 2004;22:4342-4350). Therefore, it is assumed that in an unvaccinated cohort due to a supply interruption that there would be an increase the number of infections by a factor of 2. It is estimated number of new hepatitis A virus infections estimated among children 12-23 months of age in 2006 = 3799. This estimate takes into account under reporting and asymptomatic infections (CDC Unpublished data). Without vaccine the estimated number of new hepatitis A virus infections estimated among children 12-23 months of age in 2006 = 3799 * 2 = 7598. The rate was determined utilizing the estimated population of children 12-23 months of age in 2006 = Birth Cohort of 2005 = 4,143,000 giving a rate among unvaccinated cohort of children aged 12-23 months = 183 per 100,000 persons.
Step 9: The most likely estimate is based upon data that the estimated percent morbidity (acute clinical illness) among infected children 12-23 months of age is 5.2% in 2006 (CDC Unpublished data).
Step 10: The most likely estimate is based upon an estimated death rate for children less than 5 years of age = 0%. No deaths among children less than 5 years of age was reported in 2005 or 2006 (CDC. Surveillance for Acute Viral Hepatitis – US, 2005. MMWR 2007;56. No SS-3. CDC. Surveillance for Acute Viral Hepatitis – US, 2006. MMWR 2008;57 No SS-2).
Step 11: Efficacy estimates against disease was based on clinical trial data data giving a high, low, and average efficacy estimate (Innis BL et al. Protection against hepatitis A by an inactivated vaccine. JAMA 1994:271:1328-34) (Werzberger et al. A controlled trail of a formalin-inactivated hepatitis A vaccine in healthy children. NEJM 1192;327:453-7). Efficacy estimates against hospitalization and mortality is based on no reported cases of symptomatic disease reported in children followed 9 years after vaccination (Werzberger et al. Effectiveness of hepatitis A vaccine in a former frequently affected community: 9 years' followup after the Monore field trial of VAQTA. Vaccine 2002;20:1699-701).
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the average of Havrix® (GSK) and VAQTA® (Merck) of $12.50 per dose. It does not consider the price at the time of vaccines already delivered to the stockpile.

Tetanus and Diphtheria (adolescent) Inputs:

The assumption was made to model for DTaP/Tdap utilizing pertussis inputs because pertussis has a significantly higher disease burden than diphtheria and tetanus is non-communicable. The impact from diphtheria would be difficult to quantify because of the rarity of endemic disease; no reported cases of indigenous diphtheria in the U.S. since 2000 or imported cases since 2003. Therefore, the results from a shortage of DTaP/Tdap vaccine would be detected far earlier for pertussis than diphtheria.

APPENDIX
VacStockpile Addendum – Input Assumptions

Pertussis (adolescent) Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: Tdap is a 1-dose schedule recommended at age 11-12 years.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. The 'High' target is 2 million doses (from the cohort calculation) and there are 500,000 doses of the Tdap vaccine delivered to the stockpile.
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there are 2 manufacturers (lower risk of 100% shortage), but some increased risk of supply disruptions due to a relatively recent introduction into the market and that if there are any production problems for the antigens contained in the vaccine, it is likely that they would be prioritized for the pediatric formulations. See Scenario 2 in Criteria for Shortage Probability addendum.
Step 8: The low and most likely estimates are based on reported rates from 1996-2004 among persons 11-18 years of age for the U.S. and for Massachusetts, respectively (Broder KR, Cortese MM, Iskander JK, Kretsinger K, Slade BA, Brown KH, et al. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2006;55(RR-3):1-34). The high estimate is based on data available on adolescent rates in Wisconsin in 2004 (CDC unpublished data; Davis J. Clinical and Economic Effects of Pertussis Outbreaks. *Pediatric Infectious Disease Journal*. 2005; 24(6):S109-S116.)
Step 9: The low estimate is based on reported rates in the U.S. for cases 10-19 years of age from 2001-2003 (Pertussis--United States, 2001-2003. *MMWR Morb Mortal Wkly Rep*. 2005;54(50):1283-6). The most likely estimate is based on reported adolescent rates in Massachusetts from 1989-1998 (Yih WK, Lett SM, des Vignes FN, Garrison KM, Sipe PL, Marchant CD. The increasing incidence of pertussis in Massachusetts adolescents and adults, 1989-1998. *J Infect Dis*. 2000;182(5):1409-16). The high estimate is based on reported rates in the U.S. from 1990-1996 (Guris D, Strebel PM, Bardenheier B, Brennan M, Tachdjian R, Finch E, et al. Changing epidemiology of pertussis in the United States: increasing reported incidence among adolescents and adults, 1990-1996. *Clin Infect Dis*. 1999;28(6):1230-7).
Step 10: The low estimate is based on reported rates from 1990-1996 in the U.S. among persons 10-19 years of age (Guris D, Strebel PM, Bardenheier B, Brennan M, Tachdjian R, Finch E, et al. Changing epidemiology of pertussis in the United States: increasing reported incidence among adolescents and adults, 1990-1996. *Clin Infect Dis*. 1999;28(6):1230-7). The most likely and high estimate is based on available for cases 11-19 years of age in the U.S. in 2003 and 2004 (CDC unpublished data).
Step 11: The low estimate for vaccine efficacy against disease is based on the bridging studies for Tdap from infant vaccine efficacy studies (Broder KR, Cortese MM, Iskander JK, Kretsinger K, Slade BA, Brown KH, et al. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2006;55(RR-3):1-34). The most likely and high estimate for vaccine efficacy against disease is based on a published trial among adolescents and adults (Ward JI, Cherry JD, Chang SJ, Partridge S, Lee H, Treanor J, et al. Efficacy of an acellular pertussis vaccine among adolescents and adults. *N Engl J Med*. 2005;353(15):1555-63). For vaccine effectiveness against hospitalization and death, it was assumed that some level of protection against pertussis exists in adolescents who have completed the childhood DTaP series, thereby decreasing the likelihood of hospitalization and/or death in this age group. For this model, it is assumed that the efficacy of Tdap against hospitalization and death is the same as the efficacy against incidence, primarily because even in the absence of Tdap (pre-2005), hospitalizations and deaths among adolescents were rare, so there is no available evidence of added efficacy from Tdap against these outcomes.
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the average of Boostrix® (GSK) and Adacel® (Sanofi). It does not consider the price at the time of vaccines already delivered to the stockpile.

APPENDIX
VacStockpile Addendum – Input Assumptions

Human Papilloma Virus Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: HPV vaccine is a 3-dose schedule recommended beginning at age 11-12 years.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~2 million female infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. The 'High' target is 3 million doses (from the cohort calculation). Currently there are 200,000 doses of the HPV vaccine delivered to the stockpile.
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there is 1 manufacturer (higher risk of 100% shortage), and while there has been a relatively stable and growing market a competitor HPV vaccine may be soon on the horizon and HPV is a relatively new vaccine and a steady state demand has not yet been realized. See Scenario 4 in Criteria for Shortage Probability addendum.
Step 8: Incidence rate for HPV is based on the lifetime rate of CIN 1-3 attributable to HPV 16/18 based on records from a large health plan and considering the probability of receiving catch-up vaccination after a supply interruption. The most likely estimate, low estimate, and high estimate were based upon the assumption that the probability of receiving catch-up vaccination each year from age 13 to 26 years (given no previous vaccination) is 5%, 10%, and 0%, respectively.
Step 9: Morbidity from HPV is based on the lifetime rate of cervical cancer attributable to HPV 16/18 based on the 2003 CDC's National Program on Registries and NCI's Surveillance, Epidemiology, and End Results Program and considering the probability of receiving catch-up vaccination after a supply interruption. The most likely estimate, low estimate, and high estimate were based upon the assumption that the probability of receiving catch-up vaccination each year from age 13 to 26 years (given no previous vaccination) is 5%, 10%, and 0%, respectively.
Step 10: Mortality from HPV is based on the lifetime rate of death from cervical cancer attributable to HPV 16/18 based on NCI's Surveillance, Epidemiology, and End Results Program data on the distribution of cervical cancer by state and the probability of survival by stage. The most likely estimate, low estimate, and high estimate were based upon the assumption that the probability of receiving catch-up vaccination each year from age 13 to 26 years (given no previous vaccination) is 5%, 10%, and 0%, respectively.
Step 11: Efficacy estimates are based on current models of the impact of HPV vaccination in the U.S.
Step 12: Price based on the 2008 CDC contract as of August 1, 2008 for the Gardisil® (Merck) vaccine of $100.59 per dose. It does not consider the price at the time of vaccines already delivered to the stockpile.

APPENDIX
VacStockpile Addendum – Input Assumptions

Meningococcal Inputs:

Step 1: U.S. National Center for Health Statistics, 2006. http://www.census.gov/compendia/statab/tables/08s0077.xls accessed August 6, 2008.
Step 2: MCV4 is a 1-dose schedule recommended at age 11-12 years.
Step 3: 'High' target based on cohort calculation (# of doses per schedule * ~4 million infant birth cohort * ½ year). 'Low' target based on the minimum of the current # of doses delivered to the stockpile (as of June 30, 2008) or 50% of the 'High' target. The 'High' target is 2 million doses (from the cohort calculation) and there are currently no doses of the MCV4 vaccine delivered to the stockpile.
Step 4: Based on the aggregate of the manufacturer reported doses distributed nationally for 2007.
Step 5: Range of percent of doses in shortage possible in a given year evenly split in 25% increments from 0% (no shortage) to 100% (no vaccine).
Step 6: Probability degrees of shortages in Step 5 based on the fact that there are 1 manufacturer (higher risk of 100% shortage) and a relatively stable market without recent supply problems. Despite a supply/demand mismatch early in the introduction of the vaccine, catch-up demand is likely near or at its peak and production is currently adequate. New manufacturers are likely to enter the market in the near future including vaccine for this age group and potentially infants. However, this is not currently projected to cause supply problems for vaccine for this age group. See Scenario 3 in Criteria for Shortage Probability addendum.
Step 8: The low estimate is based on the rate of A, C, Y, W-135 disease among adolescents during a low year just after the introduction of MCV4 vaccine in the U.S. (2006). The most likely estimate is based on the average annual rate over a 10 year period just prior to the introduction of MCV4 vaccine. The high estimate is based on the rate during a high year (1997). See http://www.cdc.gov/ncidod/dbmd/abcs/survreports.mening06.pdf.
Step 9: The estimate is based upon evidence that hospitalization rates among those with disease has been consistently ~90% over time.
Step 10: Case fatality rates have been stable overall for the past 20 years with the 10 year average being 11% for ACYW disease among 11-18 year olds with a yearly variation from 9% to 13%.
Step 11: The low estimate for vaccine efficacy against disease is based on an estimation from reports of vaccine failure during a time when disease rates were at a nadir. The most likely rate is based on efficacy of polysaccharide vaccine and immunogenicity equivalence studies conducted for licensure of MCV4. The high rate is based on subject matter expert best estimation. Efficacy against hospitalization and mortality is based on the assumption that vaccine prevents disease entirely (rather than modify disease).
Step 12: Price based on the 2008 CDC contract as of August 1, 2008. It does not consider the price at the time of vaccines already delivered to the stockpile.